

REMARKS

Upon entry of the amendments set forth above, Claims 1-3, 5, 6, and 9-52 are pending and presented for examination. Claims 4, 7, and 8 have been cancelled without prejudice toward future prosecution. Claims 1-3, 5, 6, 9, 10, 23, 24, 51 and 52 have been amended. Support for the amendment to claim 1 can be found, for example, in the specification at paragraphs [0042] of the published application, and original claims 7 and 8. Support for the amendment to claims 2, 3, 5, and 6 can be found, for example, in original claim 4. Support for the amendment to claims 9 and 10 can be found, for example, in original claim 8. Claim 23 has been amended to address the claim objections discussed below. Support for the amendments to Claim 52 is found, for example, in paragraphs 12, 13 and 26 of published application. Claim 52 has been amended to correct the spelling of "surface." Thus, no new matter is introduced by the amendments.

The title of the application has been amended according to the Examiner's suggestion.

Claim Objections

Claims 23 and 24 are objected to because of typographical formalities. Applicants have amended claim 23 according to the Examiner's recommendation to recite "fixing" instead of "mixing." Applicants submit that claim 24 does now properly depend from claim 1, which as amended recites "gas stream."

Rejections under Statutory Double Patenting – 35 U.S.C. § 101

Claims 1, 4, 7-14, 24-25, 30, 50, and 51 have been provisionally rejected under 35 U.S.C. § 101 as allegedly claiming the same invention as that of claims 36-45, 47, 51-53, and 57-58 of copending Application No. 10/567,193. According to the Examiner, these claims are in conflict because they claim the same invention. *Office Action*, page 3.

Applicants respectfully disagree. Amended independent claims 1 and 51 are different from the cited claims in the co-pending application. Furthermore, domination and double patenting are two separate issues. MPEP § 804. One application "dominates" a second application when the first application has a broad or generic claim which fully encompasses or reads on an invention defined in a narrower or more specific claim in another application. *Id.* Domination by itself cannot support a double patenting rejection. *In re Kaplan*, 789 F.2d 1574,

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1577-78, 229 USPQ 678, 681 (Fed. Cir. 1986); and *In re Sarrett*, 327 F.2d 1005, 1014-15, 140 USPQ 474, 482 (CCPA 1964).

Independent claim 36 of copending Application No. 10/567,193 (hereinafter “the ‘193 application”), from which claims 37-45, 47, 51-53, and 57 depend, is both different from the instant claims and is a broader claim that dominates claim 1 of the instant application and claims 1, 4, 7-14, 24-25, 30, and 50 dependent therefrom. Claim 1 of the instant application as amended recites that the molecule species in the solvent bind to the protein in the protein crystal as ligands and have a molecular weight of less than 500 Da. As such, the claims are not identical. Also, claim 36 of the ‘193 application is broader and dominates claim 1 of the instant application, but is insufficient to support a double patenting rejection under § 101.

Moreover, the cited claims of the ‘193 application and instant claims 1, 4, 7-14, 24-25, 30, and 50 do not claim the same invention. In comparing claims between two applications, statutory double patenting does not exist if an embodiment can fall within the scope of one claim but not the other. MPEP § 804. As noted above, amended claim 1 of the instant application requires that the molecule species ligands have a molecular weight of less than 500 Da. An embodiment that features ligands having a molecular weight greater than 500 Da would fall within the scope of claim 36 of the ‘193 application, but not amended claim 1 of the instant application. Also, amended claim 51 is different than the claims in the co-pending application, and therefore, is not subject to double patenting under § 101.

Thus, Applicants submit that no statutory double patenting exists and request withdrawal of the rejections of claims 1, 4, 9-14, 24-25, 30, 50, and 51 under 35 U.S.C. § 101. Claims 7 and 8, have been cancelled, rendering their rejection under 35 U.S.C. § 101 moot.

Rejections under Nonstatutory Obviousness-type Double Patenting

Claims 15, 17, 20, 26, 27, and 29 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 46, 48, 49, and 54-56 of the ‘193 application. Without acquiescing and solely to expedite prosecution, Applicants herewith file a terminal disclaimer in compliance with 37 CFR 1.321(c). Accordingly, Applicants request withdrawal of the rejection of claims 15, 17, 20, 26, 27, and 29 under nonstatutory obviousness-type double patenting.

Rejections under 35 U.S.C. § 102(b)

Claims 1-5, 7-10, 13, 14, 24, 25, 29, 32-25, 44, and 45 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Rossle *et al.* (hereinafter "Rossle"). "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." M.P.E.P. § 2131 (quoting *Verdegall Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987)).

As a preliminary matter, Rossle was published online on April 22, 2003. As such, the publication date of Rossle is less than one year before the August 6, 2003 and January 24, 2004 foreign priority dates of the instant application that the Examiner has acknowledged. Consequently, rejections based on Rossle should have been made under 35 U.S.C. § 102(a) rather than 102(b).

Nevertheless, as amended, claim 1 recites treating a protein crystal with a solution containing a solvent and one or more molecule species in the solvent, wherein the molecule species bind to the protein in the protein crystal as ligands and have a molecular weight of less than 500 Da. By contrast, Rossle merely describes hydrating crystallized chitin by using an inkjet system to apply *water* microdrops to the chitin crystal. In other words, Rossle discloses application of water alone, lacking any ligands, to a crystalline chitin sample. Claim 1 has been amended to make clear that the claimed method relates to molecule species in the solvent which bind to the protein in the protein crystal as ligands and have a molecular weight less than 500 Da.

The Examiner argues that water "can act as a ligand for protein binding." *Office Action*, page 5. Applicants disagree and contend that water is merely a solvent, which may or may not have ligands present therein. Moreover, in the context of Rossle, the water solvent does not act as a ligand for protein binding but rather merely hydrates the chitin sample. Nevertheless, claim 1 has been amended to make clear that ligands that bind protein in the protein crystal are not the solvent itself, but in the solvent. Consequently, because Rossle does not disclose any ligands in water that bind to the chitin, Rossle fails to teach the claimed limitation of one or more molecule species in the solvent that bind to the protein in the protein crystal as ligands. Accordingly, Rossle does not anticipate claim 1 and claims dependent therefrom.

Furthermore, amended claim 1 requires treating a protein crystal with a solution. Rossle, by contrast, discloses treating chitin, which is not a protein but is in fact a carbohydrate

polysaccharide. As such, Rossle does not teach the claimed limitation of treating a protein crystal.

For the foregoing reasons, Rossle fails to teach each and every limitation of independent claim 1. Accordingly, claim 1 and claims 2-5, 9, 10, 13, 14, 24, 25, 29, 32-25, 44, and 45 dependent therefrom are novel over Rossle. Applicants respectfully request withdrawal of the claim rejections under 35 U.S.C. § 102(b).

Rejections under 35 U.S.C. § 103(a) based on Rossle in view of Hasnain, Kiefersauer, Nienaber, Erlanson, and/or Huth.

Various claims dependent from claim 1 have been rejected under 35 U.S.C. § 103(a) over Rossle in view of Hasnain et al. ("Structure of metal centres in proteins at subatomic resolution," 1999) ("Hasnain"), Kiefersauer et al. ("A novel free-mounting system for protein crystals: transformation and improvement of diffraction power by accurately controlled humidity changes," 2000) ("Kiefersauer"), Nienaber et al., ("Discovering novel ligands for macromolecules using X-ray crystallographic screening," 2000) ("Nienaber"), Erlanson et al. ("Fragment-based drug discovery," 2004), and/or Huth et al. ("Utility of NMR in lead optimization: Fragment-based approaches," 2002) ("Huth"). As an initial matter, Erlanson was published on July 1, 2004, after the priority dates of the instant application, and is thus not prior art.

It is well settled that the Examiner "bears the initial burden of presenting a *prima facie* case of unpatentability..." *In re Sullivan*, 498 F.3d 1345 (Fed. Cir. 2007). Until the Examiner has established a *prima facie* case of obviousness, the Applicants need not present arguments or evidence of non-obviousness. To establish a *prima facie* case of obviousness, the Examiner must establish at least three elements. First, the prior art reference (or references when combined) must teach or suggest all of the claim limitations: "All words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson*, 424 F.2d 1382, 165 U.S.P.Q. 494, 496 (CCPA 1970); *see also M.P.E.P. § 2143.03*. Second, there must be a reasonable expectation of success. *In re Merck & Co., Inc.*, 800 F.2d 1091 (Fed. Cir. 1986); *see also M.P.E.P. § 2143.02*. And finally, the Examiner must articulate some reason to modify or combine the cited references that renders the claim obvious.

As discussed above, Rossle fails to teach each and every limitation of claim 1, at least with regard to treating a protein crystal with a solution containing a solvent and one or more molecule species in the solvent, wherein the molecule species bind to the protein in the protein crystal as ligands and have a molecular weight of less than 500 Da. These limitations are also not described in Hasnain, Kiefersauer, Nienaber, or Huth, as discussed with respect to the rejected dependent claims below.

Claim 6

Claim 6 has been rejected under 35 U.S.C. § 103(a) over Rossle in view of Hasnain. Hasnain is focused on the structure of metal centers in proteins at subatomic resolution, but does not describe applying microdrops of a solution containing ligands that bind to the protein of the protein crystal. As such, the combination of Rossle and Hasnain fails to establish a *prima facie* case of obviousness over claim 1, from which claim 6 depends. Applicants request withdrawal of the rejection of claim 6 under 35 U.S.C. § 103(a).

Claims 11, 12, 15, 16, 18, 19, 36-43, and 46-51

Claims 11, 12, 15, 16, 18, 19, 36-43, and 46-51 have been rejected under 35 U.S.C. § 103(a) over Rossle in view of Kiefersauer. Kiefersauer describes a free-mounting system for protein crystals, but does not disclose applying microdrops of a solution containing ligands that bind to the protein of the protein crystal. As such, the combination of Rossle and Kiefersauer fails to establish a *prima facie* case of obviousness over claim 1, from which claims 11, 12, 15, 16, 18, 19, 36-43, and 46-50 depend. Similarly, the cited references fail to establish a *prima facie* case of obviousness over claim 51. Applicants request withdrawal of the rejection of these claims under 35 U.S.C. § 103(a).

Claims 17 and 20-22

Claims 17 and 20-22 have been rejected over Rossle in view of Kiefersauer in further view of Nienaber. As discussed above, Rossle and Kiefersauer fail to disclose applying microdrops of a solution containing ligands that bind to the protein of the protein crystal. This missing limitation is also lacking in Nienaber, which describes methods for discovering novel

ligands using X-ray crystallographic screening. In Nienaber, the screening method is based on a soaking technique in which the crystallized sample is submerged in a bath containing chemical fragments. *Nienaber*, Figure 1. Electron density maps are compared before and after soaking the crystal to identify binding sites of the chemical fragments to the sample. As such, Nienaber fails to disclose applying microdrops of a solution containing ligands that bind to the protein of the protein crystal, but rather instructs to submerge them in a bath.

Furthermore, because the soaking method is central to screening method of Nienaber, Nienaber actually teaches away from the instant claims and combination with Rossle. One of ordinary skill in the art guided by Nienaber to submerge a crystal in a bath containing chemical fragments would be actively discouraged from applying microdrops to a crystal fixed on a holding device without being embedded in a liquid environment as claimed. Furthermore, one of ordinary skill would not perform the hydration method of Rossle in view of Nienaber, which instructs to soak the crystal. For the foregoing reasons, the combination of Rossle, Kiefersauer, and Nienaber fails to establish a *prima facie* case of obviousness over claim 1, from which claims 17 and 20-22 depend. Applicants request withdrawal of the rejection of these claims under 35 U.S.C. § 103(a).

Claims 23 and 52

Claims 23 and 52 have been rejected over Rossle in view of Erlanson. As noted above, Erlanson was published after the priority dates of the instant application and is thus not prior art. Claims 23 and 52 have also been rejected over Rossle in view of Huth, which describes NMR lead optimization, but does not disclose applying microdrops of a solution containing ligands that bind to the protein of the protein crystal. As such, the combination of Rossle and Huth fails to establish a *prima facie* case of obviousness over claim 1, from which claims 23 and 52 depend. Applicants request withdrawal of the rejection of these claims under 35 U.S.C. § 103(a).

Claims 26 and 28

Claims 26 and 28 have been rejected over Rossle in view of Nienaber. As discussed above, the combination of Rossle and Nienaber fails to establish a *prima facie* case of

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obviousness over claim 1, from which claims 26 and 28 depend. Applicants request withdrawal of the rejection of these claims under 35 U.S.C. § 103(a).

Claim 27

Claim 27 has been rejected over Rossle in view of Nienaber in further view of Hasnain. As discussed above, Rossle, Nienaber, and Hasnain each fail to disclose applying microdrops of a solution containing ligands that bind to the protein of the protein crystal. Consequently, the combination of these references fails to establish a *prima facie* case of obviousness over claim 1, from which claim 27 depends. Applicants request withdrawal of the rejection of claim 27 under 35 U.S.C. § 103(a).

Claim 30

Claim 30 has been rejected over Rossle. As discussed above, Rossle fails to disclose applying microdrops of a solution containing ligands that bind to the protein of the protein crystal, and thus fails to establish a *prima facie* case of obviousness over claim 1, from which claim 30 depends. Applicants request withdrawal of the rejection of claim 30 under 35 U.S.C. § 103(a).

Claim 31

Claim 31 has been rejected over Rossle in view of Kiefersauer in further view of Nienaber in still further view of Erlanson or Huth. As discussed above, Rossle, Kiefersauer, Nienaber, and Huth each fail to disclose applying microdrops of a solution containing ligands that bind to the protein of the protein crystal, and Erlanson is not prior art. Consequently, the combination of these references fails to establish a *prima facie* case of obviousness over claim 1, from which claim 31 depends. Applicants request withdrawal of the rejection of claim 31 under 35 U.S.C. § 103(a).

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CONCLUSION

Applicants have endeavored to address all of the Examiner's concerns as expressed in the outstanding Office Action. In light of the above amendments and remarks concerning the pending claims, Applicants respectfully request issuance of a Notice of Allowance. If the Examiner has any questions which may be answered by telephone, the Examiner is invited to call the undersigned directly.

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, Applicant is not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. Applicant reserves the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that Applicant has made any disclaimers or disavowals of any subject matter supported by the present application.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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